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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,632	01/14/2004	Bianca Baroli	0492611-0520	4661

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EXAMINER	
BARNHART, LORA ELIZABETH	

ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
06/03/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@choate.com

Office Action Summary	Application No.	Applicant(s)	
	10/757,632	BAROLI ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,6,12,21,22,25-31,56,57 and 82-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,6,12,21,22,25-31,56,57 and 82-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/19/08 has been entered.

Response to Amendments

Applicant's amendments filed 3/19/08 to claims 1, 3, 12, 21, 25, 29-31, 56, and 57 have been entered. Claims 32, 33, 39, 48, 49, 52-55, 58-62, 73, 74, and 77-81 have been cancelled in this reply. Claims 82-84 have been added. Claims 1, 3, 6, 12, 21, 22, 25-31, 56, 57, and 82-84 remain pending in the current application, all of which are being considered on their merits. Prior art references not included with this Office action can be found in a prior action.

Election/Restrictions

Applicant's election with traverse of the species "tissue engineering," "gelatin," "protein," "sugar," "polyethylene glycol," "cross-linked synthetic polymer," "granulation," "visible radiation," and "dissolution-controlled systems" in the reply filed on 4/23/07 is still in effect over the claims.

Claim Rejections - 35 USC § 112

Any rejections of record under 35 U.S.C. § 112, second paragraph, not specifically addressed below are withdrawn in light of the claim amendments.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition that repairs or restructures tissue when administered to an organism, does not reasonably provide enablement for a composition that replaces tissue per se. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQd 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

Claim 3 is drawn in part to a composition that replaces tissue in an organism. Tissue, by definition, is a composition comprising an aggregate of cells and their

supportive matrix (see reference U, http://www.merriam-webster.com/dictionary/tissue). Therefore, a composition that replaces tissue necessarily includes cells. Claim 1 does not include cells, and the specification does not appear to contemplate embodiments in which cells are placed into the instantly claimed composition. While a singular, narrow working embodiment cannot be a sole factor in determining enablement, its limited showing, in light of the unpredictable nature of the art and the lack of direction applicants present, provides additional weight to the lack of enablement in consideration of the *Wands* factors as a whole. Thus, one of ordinary skill in the art would not have a reasonable expectation of success in using the claimed invention across its entire scope.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 6, 12, 21, 22, 25-31, 56, 57, and 82-84 are/remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a composition comprising "photopolymerizable monomers" and a material insoluble by the monomers "that is solid at below the body temperature of a living organism and a gel at the body temperature of a living organism," which is confusing. It is not clear whether the instant composition responds to light, temperature, or both. Clarification is required.

Claim 1 also requires that the insoluble material "shields the bioactive molecules from a polymerization process," but the nature and extent of this shielding is not clear. Clarification is required.

Claim 1 requires that the monomers "cross-link to form a polymer," but the conditions for this cross-linking are not limited in the claim. Clarification is required.

Independent claims 83 and 84 suffer similar deficiencies and are rejected on the same grounds. Because claims 3, 6, 12, 21, 22, 25-31, 56, 57, and 82 depend from indefinite claim 1 and do not clarify these points of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim 3 allows that the composition can "replace" tissue in an organism. It is not clear how the composition of claim 1 as claimed can actually replace tissue, since there are no cells in the composition, and cells cannot reasonably be considered "bioactive molecules." Tissue necessarily includes cells. Clarification is required.

Claim 31 requires that the photopolymerization means in claim 30 "uses visible radiation." Since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 83 refers to a "new system," which is confusing. Clarification is required. The word "new" should not appear in patent claims.

Claim 84 recites the limitation "the monomers material" in line 4, but there is no antecedent basis for this limitation. Clarification is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 6, 12, 21, 22, 25-28, 30, 31, 57, 82, and 83 are/remain rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al. (2003, U.S. Patent Application Publication 2003/0236573).

Evans teaches a flowable implant for treating tissue defects (paragraphs 139 and 140, e.g.). The composition of Evans may include a growth factor (i.e., a bioactive protein), gelatin (which is both an insoluble material and a bioactive protein), and a photopolymerizable monomer (e.g., FOCALSEAL) (see paragraph 139). Evans contemplates an embodiment in which the implant treats a tissue defect only at body temperature (paragraphs 127 and 139). The composition of Evans may further include polyethylene glycol as a filler (Table 4 at paragraph 7) and may include plasticizers other than polyethylene glycol, many of which are also cross-linked synthetic polymers (Table 5 at paragraph 108). The composition of Evans may comprise sugars (paragraph

171). The composition of Evans may include any of numerous components (Table 5 at paragraph 109). The composition of Evans is a "drug-loaded delivery system [that] delivers the bioactive materials to a living organism' in that Evans teaches that the composition is suitable for introduction into a body for therapeutic purposes (paragraph 140, e.g.).

The limitations "wherein the binder binds the insoluble material to protect the bioactive molecules" (claims 21 and 48), "wherein the plasticizer increases the flexibility of the cross-linked structure" (claims 25 and 52), and "wherein the disaggregant aids with the solid-gel transition" (claims 27 and 54) all recite inherent properties of these components. A plasticizer, by definition, increases the flexibility of compositions. These limitations do not describe these components in structural terms. The limitations "wherein the insoluble material protects the bioactive molecules" (claims 1 and 32) and "wherein the granules protect the bioactive molecules" (claims 29 and 56) do not particularly point out the nature of the protection; a composition comprising an insoluble material and bioactive molecules necessarily "protects" at least some of the bioactive molecules, since at least some of them are mixed with the insoluble material and "protected" from the air, as opposed to a composition consisting of bioactive molecules only.

A person of ordinary skill in the art would have had a reasonable expectation of success in making a composition comprising a bioactive protein, a photopolymerizable monomer, a insoluble material insoluble in the monomers, a binder such as a sugar, a plasticizer such as polyethylene glycol, any of numerous cross-linked synthetic

polymers, granules of any of numerous components, and a photopolymerization means such as the light in the laboratory because Evans teaches that all of these components may be included in a flowable implant that may be administered into a patient's body to treat a tissue defect. The selection of the components and the amounts thereof would have constituted routine optimization on the part of the person of ordinary skill in the art, said artisan recognizing that Evans teaches that the composition may be modified to be compatible with the defective tissue being treated and to mimic said tissue's properties (paragraph 110, e.g.). The disclosure of Evans is broad and inclusive; Evans contemplates optimization of the components to be included and the conditions to be treated (paragraph 113, e.g.). A holding of obviousness over the cited claims is therefore clearly required. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Applicants allege generally that Evans does not teach the claimed invention and does not provide a suggestion to modify the invention as discussed in the rejection (Reply, page 7, last paragraph; and page 8, paragraph 1). Applicants allege that the instant composition has properties that Evans's composition does not have, specifically a shielding effect against some type of "deleterious" environment (Reply, page 8, paragraph 1). Applicants allege that Evans "does not provide any structural limitations for overcoming the deleteriousness of the polymerizing environment" (ibid.). These arguments have been fully considered, but they are not persuasive.

In the recent decision *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007), the Supreme Court determined that a demonstration of a teaching, suggestion, or motivation provides a "helpful insight" in determining obviousness (see *KSR* at 14). In the paragraph immediately after this one, however, the Court points out, "Helpful insights, however, need not become rigid and mandatory formulas ... The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents. The diversity of inventive pursuits and of modern technology counsels against limiting the analysis in this way" (see *KSR* at 15). The gist of *KSR* is that no such explicit suggestion need be present in the art for a proper rejection under 35 U.S.C. § 103. The fact that Evans does not explicitly suggest the particular combination of ingredients in the instant composition is insufficient to overcome the obviousness rejection.

Applicants' arguments amount to an allegation that they have identified that the composition suggested by Evans could be used for a purpose not specifically contemplated by Evans and that the composition of Evans has advantageous properties that were not explicitly discussed in the reference. The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Evans suggests combining the components instantly recited, and Evans is analogous art to the instant invention. Applicant has supplied no evidence that the

instant composition as claimed possesses properties that would not flow naturally from following the suggestion of Evans to combine the components.

Applicants make reference to a "deleterious" environment, but it is still not clear why the instantly claimed invention would necessarily protect from such an environment and the composition suggested by Evans would not. The claims are broad; claim 1 puts no limit on the character of the monomers or the insoluble material, and claim 1 does not limit the type of bioactive molecules being "protected." The nature of the stress of the polymerizing environment is not clear, and the manner in which the instantly claimed invention protects against such stress is not clear. The specification includes a working example in which two enzymes are shown to retain more activity over a few days when suspended in polyethylene glycol dimethacrylate (PEGDM) that includes ethyl 4-dimethylaminobenzoate (EDMAB) and camphorquinone (CQ) (a photopolymerizing monomer and its activator) as compared to enzymes suspended in PEGDM alone (see page 15, line 21, et seq.). However, this extremely limited showing cannot constitute a showing of unexpected results across the entire scope of the claims. None of the claims limits the "bioactive molecules" to enzymes, and none of the claims limits the "protection" to retention of enzyme activity. Amending the claims to so limit them might advance prosecution.

Regarding applicants' allegation that Evans does not provide "structural limitations for overcoming the deleteriousness of the polymerizing environment," it is respectfully submitted that most of the instant claims also provide no such structural limitations. Claim 1 describes the insoluble material and the monomers exclusively

using functional language. Claims 6 and 83 limit the insoluble material to gelatin, and claim 12 limits the bioactive material to proteins, but otherwise, the claims describe the components solely in terms of their function.

Claims 29, 56, and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans (2003, U.S. Patent Application Publication 2003/0236573) as applied to claims 1, 3, 6, 12, 21, 22, 25-28, 30, 31, 57, 82, and 83 above, and further in view of Kaetsu et al. (1982, U.S. Patent 4,359,483; reference A).

The teachings of Evans are relied upon as above. Evans does not exemplify a composition that comprises granules per se.

Kaetsu teaches granulated compositions in which one active agent is encapsulated in another (column 1, line 50, through column 2, line 24). Kaetsu teaches that the encapsulating component may be gelatin (column 2, lines 38-52) and that the active agent may be proteins or enzymes (column 3, lines 40-60). The system of Kaetsu is compatible with photopolymerizable systems (column 3, lines 19-39). Kaetsu teaches that granules comprising these components promote slow release of the active agent (column 2, lines 21-23).

A person of ordinary skill in the art would have had a reasonable expectation of success in granulating or encapsulating the active components within the composition of Evans because Kaetsu teaches that such states of matter are compatible with photopolymerizable systems. The skilled artisan would have been motivated to encapsulate or granulate one or more of the components of Evans because Kaetsu

teaches that such states of matter facilitate sustained release of the active agent, thereby prolonging the period of time for which it is therapeutic.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to granulate or encapsulate one or more of the components in the composition of Evans because Kaetsu teaches that encapsulated granules were well known in the art at the time of the invention for promoting sustained release of active agents.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Applicants' comments regarding the rejections of record have been considered to the extent they read on this ground of rejection, but none of the comments specifically addresses the inventiveness of granulated particles within the composition.

No claims are allowed. No claims are free of the art.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, **not** the published application. Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lora E Barnhart/
Primary Examiner, Art Unit 1651